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Recovery of visual field constriction following discontinuation of vigabatrin

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Epilepsy patients treated with vigabatrin may develop symptomatic or asymptomatic concentric visual field constriction due to GABA-associated retinal dysfunction. The prevalence and course of this side effect are not established yet; in previously reported adult patients the visual disturbances seem to be irreversible. We present two patients with a significant improvement of visual field constriction and retinal function after the discontinuation of vigabatrin. These findings suggest that vigabatrin-associated retinal changes are at least partly reversible in some patients, and that these patients may benefit significantly from a withdrawal of vigabatrin. Larger scale clinical studies are needed to identify predictive factors both for the occurrence and reversibility of vigabatrin-associated visual field defects.

Key words: epilepsy; vigabatrin; visual field construction; antiepileptic drugs; adults.

INTRODUCTION

Since Eke *et al*'s first report of severe symptomatic visual field defects in patients taking vigabatrin in 1997[1], many features of this particular side effect remain unclear. The prevalence of clinical and subclinical visual field defects under vigabatrin therapy is not established yet, and it is not known if these disturbances are related to the dose or the duration of vigabatrin exposure, interactions with other antiepileptic drugs, the age of the patient or the type or severity of epilepsy[1–6]. To judge the risk versus benefit of a vigabatrin therapy[7], the question about the course of the visual field defects is crucial. In the vast majority of reported cases the visual field defects failed to resolve if vigabatrin was stopped. Of the two previously reported cases with reversibility of visual field defects after discontinuation of vigabatrin, one was an atypical unilateral deficit ascribed to an allergic vasculitis[8], the second occurred in a 10-year-old child[9]. We present two adult patients with specific features of symptomatic vigabatrin-associated visual field defects with a significant recovery after the withdrawal of the drug. Results of visual field examinations and electroretinograms (ERG) are provided.

PATIENTS

Patient 1: A 64-year-old man with 43 year history of complex partial seizures had been treated with vigabatrin 1500 mg/day in addition to his long-standing therapy with carbamazepine 800 mg/day. Two years after starting vigabatrin the patient noted gradual non-specific visual disturbances. Ophthalmological assessment showed a bilateral concentric constriction of the visual fields which progressed further over the next 20 months until vigabatrin was stopped (Fig. 1a). ERG demonstrated bilateral increased a-wave latency to bright light flash (mixed rod-con response), unrecordable oscillatory potentials, abnormal phase 30 Hz flicker response and subnormal pattern ERG, indicative of generalized cone dysfunction in both eyes. The light rise of the electrooculogram was also subnormal bilaterally.

Ophthalmological assessments one and six months after vigabatrin was discontinued revealed a bilateral significant improvement of the visual field defect and the ERG (Fig. 1b).

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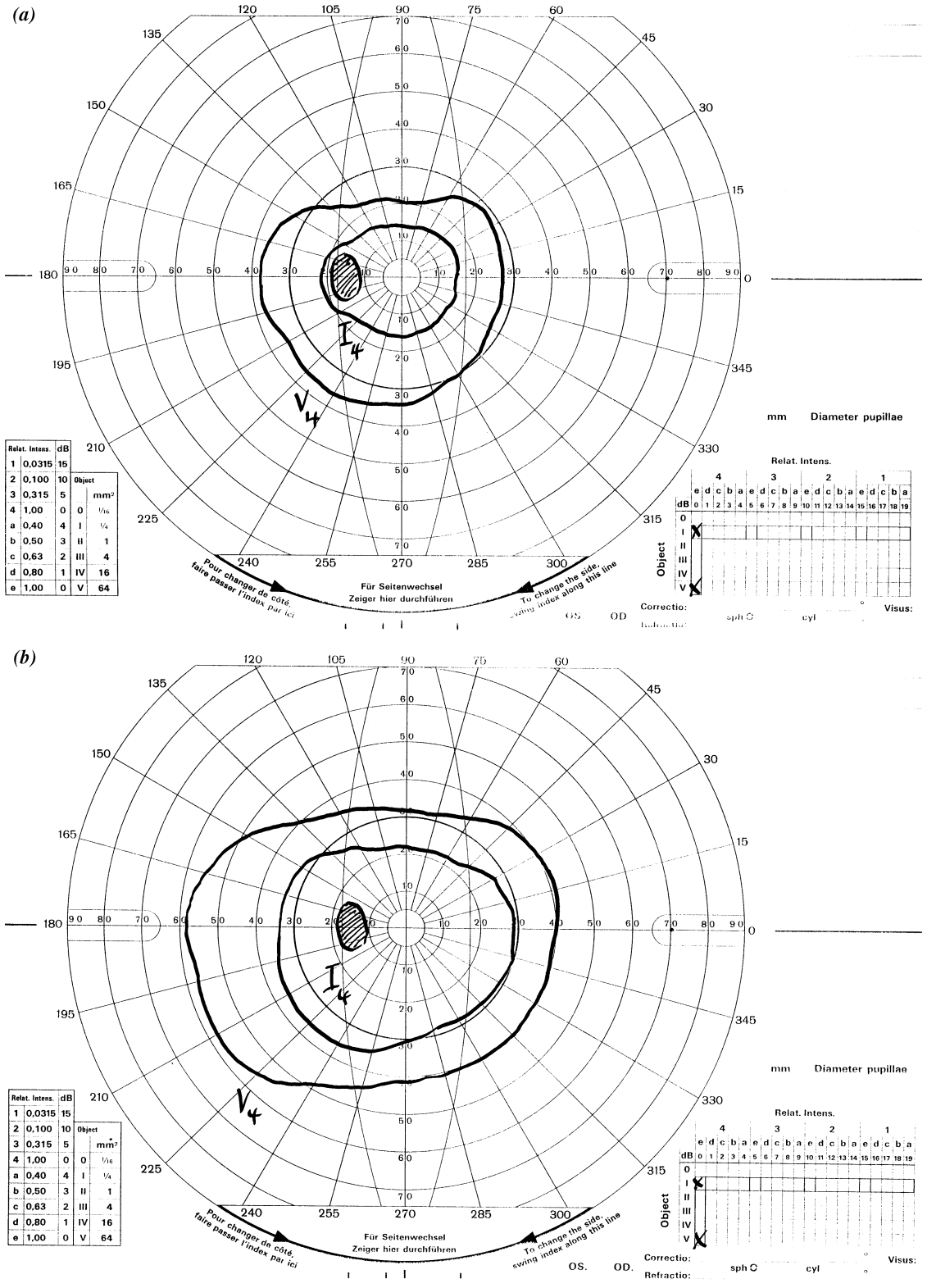

Fig. 1: (a) Goldman visual fields of patient 1 before vigabatrin therapy was stopped. (b) Visual fields showed an improvement six months after vigabatrin was stopped. Presented are the results of the left eye, those of the right eye are similar.

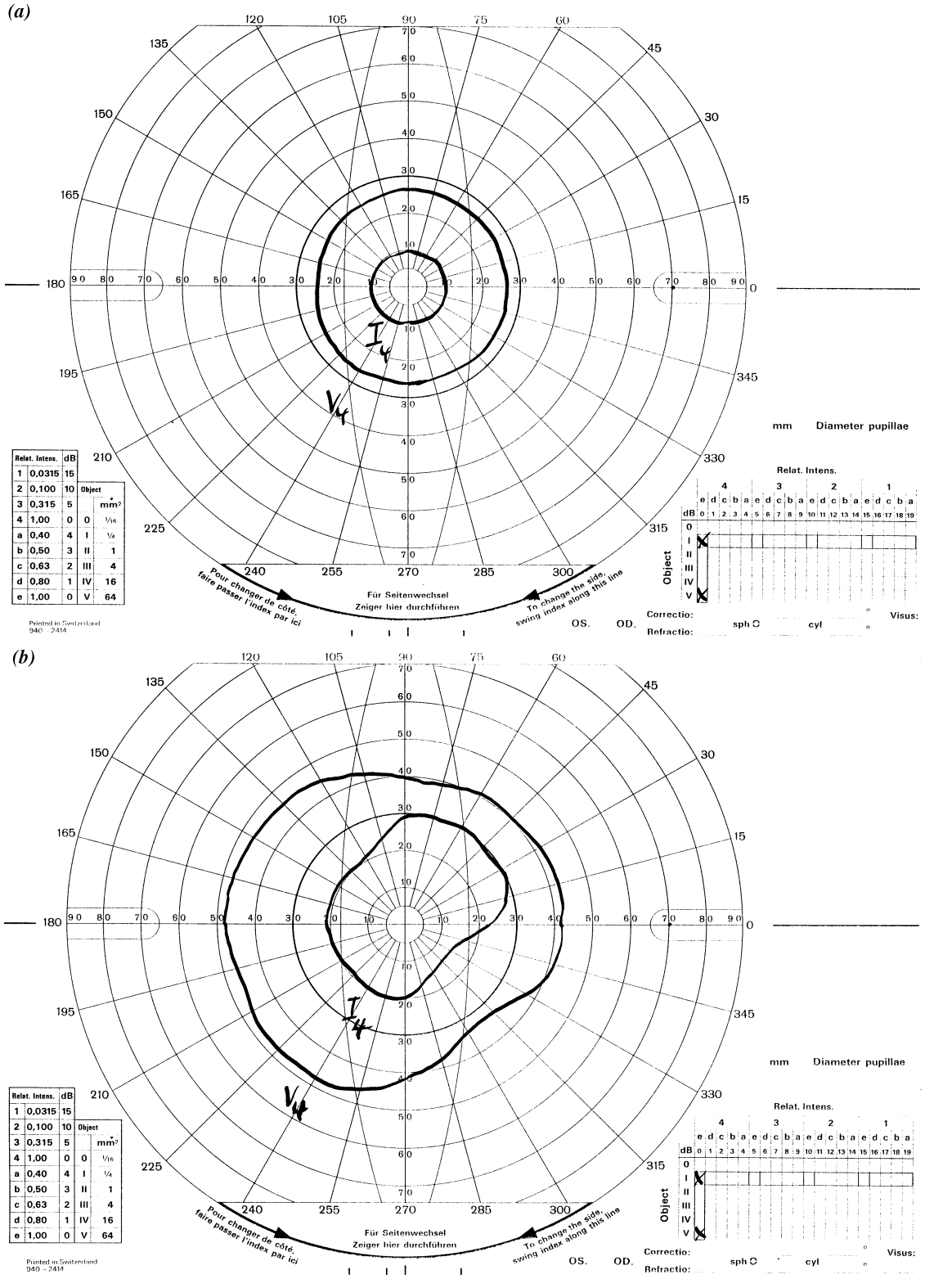

Fig. 2: (a) Goldman visual fields of patient 2 after seven and a half years of vigabatrin therapy. (b) Visual fields of patient 2 four weeks after vigabatrin was stopped. Presented are the results of the left eye, those of the right eye are similar.

Patient 2: A 37-year-old man with complex partial seizures since age 14 had been treated with up to 3500 mg vigabatrin in addition to his standard antiepileptic medication consisting of phenytoin, clobazam and felbamate. Seven years after vigabatrin was started ophthalmological assessment for intermittent peri-orbital pain revealed marked bilateral symmetrical visual field constriction (Fig. 2a). ERG abnormalities included unrecordable oscillatory potentials and borderline abnormal responses to 30 Hz white stimulation. These findings improved significantly within four weeks of stopping the drug six month after the first examination (Fig. 2b).

DISCUSSION

Concentrically constricted visual fields are an uncommon finding in the general population and in epilepsy patients treated with standard antiepileptic drugs, but occur in as many as 40% of epilepsy patients treated with vigabatrin monotherapy[6]. The two presented cases showed the typical clinical features of vigabatrin-related retinal dysfunction as described in previous reports[1]. The ERG revealed a preferential cone system dysfunction and reduced response of the highly GABAergic amacrine cells as reported earlier by Krauss *et al.*[10]. The rapid recovery of the visual fields after the discontinuation of vigabatrin confirms a primary role of the drug in the pathogenesis of retinal dysfunction. Vigabatrin seems to have the potential to damage selectively retinal GABAergic cells, presumably by the high levels of GABA resulting from the inhibition of GABA transaminase. It remains unclear, however, why the majority of patients remain free of symptoms, why some patients develop irreversible, and others reversible visual impairment. The findings in patient 2 suggest that visual field defects can be reversible in adult patients even after a vigabatrin exposure for several years with a relatively high dose.

These case-reports indicate that some patients with symptomatic visual defects may benefit significantly from a withdrawal of vigabatrin. In other epilepsy patients, namely with subclinical or mild visual field defects and a good seizure control, risks from uncontrolled seizures may out-weight risks of persistent retinal damage. In some of these patients, a reduced dose may slow down or stop the progress of the visual complications[4]. Further research is required to: (1) determine the prevalence and course of retinal dysfunction associated with vigabatrin therapy, and (2) clarify which factors determine the retinal vulnerability and the reversibility of symptoms.

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